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# Somatic Accumulation of GluA1-AMPA Receptors Leads to Selective Cognitive Impairments in Mice

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## Abstract

© 2018 Bannerman, Borchardt, Jensen, Rozov, Haj-Yasein, Burnashev, Zamanillo, Bus, Grube, Adelmann, Rawlins and Sprengel. The GluA1 subunit of the L-α-amino-3-hydroxy-5-m-thyl-4-isoxazolepropionic acid receptor (AMPAR) plays a crucial, but highly selective, role in cognitive function. Here we analyzed AMPAR expression, AMPAR distribution and spatial learning in mice (Gria1R/R), expressing the “trafficking compromised” GluA1(Q600R) point mutation. Our analysis revealed somatic accumulation and reduction of GluA1(Q600R) and GluA2, but only slightly reduced CA1 synaptic localization in hippocampi of adult Gria1R/R mice. These immunohistological changes were accompanied by a strong reduction of somatic AMPAR currents in CA1, and a reduction of plasticity (short-term and long-term potentiation, STP and LTP, respectively) in the CA1 subfield following tetanic and theta-burst stimulation. Nevertheless, spatial reference memory acquisition in the Morris water-maze and on an appetitive Y-maze task was unaffected in Gria1R/R mice. In contrast, spatial working/short-term memory during both spontaneous and rewarded alternation tasks was dramatically impaired. These findings identify the GluA1(Q600R) mutation as a loss of function mutation that provides independent evidence for the selective role of GluA1 in the expression of short-term memory.

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## Keywords

AMPA receptors, GluA1, Long-term potentiation, Morris water-maze, RNA-editing, Spatial memory, Spatial working memory

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